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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/710,058	11/10/2000	David Anderson	A-68531-1/RMS/JJD/SPL	4112

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EXAMINER	
CELSA, BENNETT M	

ART UNIT	PAPER NUMBER
1639	

DATE MAILED: 01/13/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/710,058	ANDERSON ET AL.	
	Examiner	Art Unit	
	Bennett Celsa	1639	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *30 December 1899*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-3,16 and 20* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-3,16 and 20* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. §§ 119 and 120

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

13)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application) since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

a) ☐ The translation of the foreign language provisional application has been received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121 since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *11/7/03*.
4) ☐ Interview Summary (PTO-413) Paper No(s). _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 11/7/03 has been entered.

2. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Status of the Claims

Claims 1-3, 16, and 20 are currently pending and under consideration (to the extent of the elected invention.).

Election/Restriction

3. Applicant's election without traverse of Group I (claims 1-9) and the species rGFP in Seq. Id. 1 in Paper No. 10 is again acknowledged.

Withdrawn Objection (s) and/or Rejection (s)

Applicants amendment and arguments relating thereto have overcome the following rejections:

a. Claims 1-9 are rejected under 35 U.S.C. 102(b) as being anticipated by Aran et al. Cancer Gene Ther. (July/Aug 1998) pages 195-206 and the specification description (pages 5-6 and Fig. 1) as evidence to demonstrate inherency regarding ability of reference DNA structure to be "fluorescent rGFP variant".

b. Claims 4-6 are rejected under 35 U.S.C. 102(b) as being anticipated by Abedi et al. Nuc. Acid Res. Vol. 26, No. 2 (1998) and the specification description (pages 5-6 and Fig. 1) as evidence to demonstrate inherency regarding ability of reference DNA structure to be "fluorescent rGFP variant". .

c. Claims 1-9 are rejected under 35 U.S.C. 102(e) as being anticipated by Anderson et al. US Pat. No. 6,180,343 (1/01: filed 10/98) and the specification description (pages 5-6 and Fig. 1) as evidence to demonstrate inherency regarding ability of reference DNA structure to be "fluorescent rGFP variant".

d. Claims 4-6, 9 and 17-19 are rejected under 35 U.S.C. 102(e) as being anticipated by Bryan et al. US Pat. No. 6,232,107 (5/01: filed 10/98 or earlier)with attached Result 4 DATABASE Alignment search.

Outstanding Objection (s) and/or Rejection (s)

Claim Rejections - 35 USC § 112

4. Claims 2, 3, 16 and 20 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention (lack of written description).

In this regard, applicant is referred to the case of *University of California v. Eli Lilly & Co.*, 119 F.3d 1559, 43 USPQ2d 1398 (Fed. Cir. 1997) and the "Guidelines for Examination of Patent Applications Under the 35 USC 112, first paragraph, 'Written Description' Requirement" published in 1242 OG 168-178 (January 30, 2001).

The present claims are directed to a retroviral vector (and a cell comprising) comprising a "first gene" and IRES site and polynucleotide encoding a GFP having a sequence that is 95% identical to seq. Id 2/5. *Accordingly, the presently claimed invention includes: Additional undefined genetic structure encoding additional amino acids to the C- and/or N-terminus region of the protein of seq. Id # 2/5* including continuous or discontinuous regions encoding the protein of seq. Id # 2/5 which encompasses the "gene" and those coding or non-coding sequences.

In support thereof, the specification description is directed to a specific nucleotide sequence (e.g. seq. 1) that encodes green fluorescent proteins of specific peptide sequence (e.g. amino acid content and length) and fusion constructs that further comprise polynucleotides encoding random peptides (e.g. candidate bioactive agents). There is no specification disclosure for "a first gene" or representative support thereof.

The written description provision of 35 USC 112, first paragraph. Vas-Cath Inc. v. Mahurkar, 19 USPQ2d 1111, makes clear that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention*. The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed.*" (See page 1117.)

Applicants have not described nor disclosed nucleotide structure (e.g.the "operon") which constitutes "a (first) gene" A gene is broadly defined in the art as a segment of DNA involved in the production of a polypeptide and which includes regions preceding and following the coding regions (i.e. leader and trailer) as well as regions in between individual coding segments (eg. Introns). The specification fails to describe the

functional gene *per se* (i.e., operon) which applicants have intended to be encompassed by the term "a first gene"of the instant claims as set forth *supra*.

Moreover, the claims encompass open reading frames which are 3' and 5' to the polynucleotide sequence of SEQ ID NO: 2/5, such 5' and 3' information inclusive of the definition of an operon. These regulatory and other gene sequences of the operon that are not described, are essential to the function of the gene within the operon and are therefore essential elements. Such sequences fail to have an adequate written description in the instant specification. The specification does not provide written description support for any flanking nucleic acid sequences which are 5' or 3' of SEQ ID 2/5. Since, applicants have not disclosed any information which is 3' and 5' to the polynucleotide sequence of 2/5 corresponding to "a first gene" the specification clearly lacks written description for the broad class of polynucleotides comprising polynucleotide sequence 95% identical to SEQ ID NO:2/5 which further include "a first gene"..

The actual structure or other relevant identifying characteristics of each nucleic acid that is "a first gene" (with unclaimed peptide name/properties) can only be determined empirically by actually making every nucleic acid that encodes the recited protein and testing each to determine whether it encodes a protein having the particularly disclosed properties. As noted in the Guidelines at Section IIA(2):

> There is an inverse correlation between the level of predictability in the art and the amount of disclosure necessary to satisfy the written description requirement. For example, if there is a well-established correlation

between structure and function in the art, one skilled in the art will be able to reasonable predict the complete structure of the claimed invention from its function.

The specification fails to teach the structure or relevant identifying characteristics of a representative number of "first gene" species and/or a representative number of unclaimed proteins encoded by said "first gene sufficient to allow one skilled in the art to determine that the inventor had possession of the invention as claimed.

Discussion

Applicant's amendment and arguments directed to the above rejection were considered, but deemed nonpersuasive for the following reasons. Initially, it is noted that the above rejection was modified in response to applicant's amendment.

Applicant arguments directed to claim 1 and the portion of the fusion protein of claim 2 corresponding to the seq. Id 2/5 portion has been found persuasive. However, the above rejection has been rewritten to address the term "first gene" to which these arguments are rendered moot.

As pointed out in the revised rejection above the specification fails to disclose either a representative number of "genes" falling within the scope of the genus of "first genes" or a recitation of structural features common to the members of this genus of "first genes".

Applicant argues that not all species are required to be disclosed to demonstrate possession of a genus. This argument is not persuasive since the specification fails to provide adequate specification support for critical nucleotide structure constituting a "first gene" or any species relating thereto. Compound structure which is shown to be critical or essential to the practice of the invention, such as possession of nucleic acid structure (e.g. "operon" as discussed in the rejection above) but not included in the claim(s) render the claims nonenabled and unsupported by the disclosure. See In re Mayhew, 527 F.2d 1229, 188 USPQ 356 (CCPA 1976); Ex parte Bhide (BdPatApp&Int) 42 USPQ2d 14.

The above rejection suggests claim language (e.g. a first encoding polynucleotide instead of a "first gene") which may facilitate withdrawal of the above rejection.

Accordingly, the above modified rejection is hereby maintained.

Claim Rejections - 35 USC § 103

5. Claims 1-3 and 16 are rejected under 35 U.S.C. 103(a) as being unpatentable over Bryan et al. US Pat. No. 6,232,107 (5/01: filed 10/98 or earlier)with attached Result 4 DATABASE Alignment search and Aran et al. Cancer Gene Therapy, Vol. 5, No. 4 pages 195-206 (1998). .

Bryan et al. disclose and claim the use (e.g. diagnostics and "high throughput screening" e.g. libraries) of nucleic acid molecules encoding green fluorescent proteins (e.g. bioluminscent) from the genus Renilla, including reference Seq. ID No. 15 which is 98.4% (with best local similarity of 99.4%) homologous to elected seq. ID 1, differing by

only one nucleotide (C vs. G) and reference Seq. Id. No. 16 which has 100% sequence identity to the presently claimed Renilla GFP of Seq. Id. 2. See e.g. Reference Seq. Id 15 and attached Result 4 DATABASE Alignment search; and Reference sequence Id. 16. . Bryan et al. teach the use of the bioluminescent green fluorescent proteins in cellular assays (e.g. live cells, including mammalian) and in high throughput screening systems (e.g. employing libraries) (e.g. see col. 2-3; 14). The reference further teaches the use of a "fusion partner" (e.g. a targetting agent as "a first gene") in its genetic fusion constructs. See e.g. col. 24. . Although teaching green fluorescent proteins from other sources, the use of renilla green fluorescent proteins is "more ideal for use as an analytical tool" (e.g. see col. 4-5); see also patent claims directed to Renilla sequence Id 15 and 16.

The Bryan et al. reference differs from the presently claimed invention (e.g. see claim 1) in failing to explictly teach the use of a retrovirus as a vector; and the use of "human codon optimized nucleic acid encoding a Renilla GFP"(see claim 20).

However, the Bryan et al. reference clearly teaches vectors:

a. "the [S]election and use of such vehicles" as being "well within the skill of the artisan"; and

b. in mammalian hosts including "recombinant *virus*" , as well as plasmid and phages. See e.g. col. 23 (especially bottom) to col. 24.

But, the Aran et al. reference teaches the favorable use of retroviral vectors, both in vitro and in vivo including an internal ribosome entry site (IRES) for fusion constructs preferably comprising "optimized, humanized" (e.g. see page 204, left column for

benefits of humanizing) GFP (e.g.*Aequorea victoria*) ; since "[T]his vector allows rapid and specific identification of the expressed protein (e.g. MDR1 gene transfer) in living cells (e.g. mammalian cells) ..." (E.g. see Abstract and page 195, especially right column).

Accordingly, it would have been obvious to one of ordinary skill in the art at the time of applicant's invention to utilize a retroviral vector as the "recombinant virus" vector and a humanized GFP disclosed for use in the Bryan et al. reference in order to appreciate the benefits thereof ; e.g. rapid and specific identification of the expressed protein.

6. Claims 1-3, 16 and 20 are rejected under 35 U.S.C. 103(a) as being unpatentable over Aran et al. Cancer Gene Therapy, Vol. 5, No. 4 pages 195-206 (1998) and Bryan et al. US Pat. No. 6,232,107 (5/01: filed 10/98 or earlier)with attached Result 4 DATABASE Alignment search.

Aran et al. (e.g. see abstract and entire article) disclose and teach retroviral vectors which "comprise" an "optimized , humanized" (compare to present claim 20) GFP gene (e.g. a red-shifted green fluorescent protein from *Aequorea victoria*) and which further include a "first gene" (e.g. for multridrug resistance: MDR) and an internal ribosome entry site (e.g. IRES) which is expressed in living cells (e.g. "A cell" ie. mammalian as presently claimed); along with Beta galactosidase.

Although teaching the use of an *Aequorea victoria* GFP gene sequence in its vector/fusion constructs/libraries, the Aran et al. Reference differs from the presently

claimed invention (e.g. claims 14-19) by failing to explicitly teach the use of a *Renilla* GFP gene sequence which encodes a GFP that is at least 90%, 95%, 100% identical to SEQ Id. 2.

However, Bryan et al. disclose and claim the use (e.g. diagnostics and "high throughput screening" e.g. libraries) of nucleic acid molecules encoding green fluorescent proteins (e.g. bioluminscent) from the genus Renilla, including reference Seq. ID No. 15 which is 98.4% (with best local similarity of 99.4%) homologous to elected seq. ID 1, differing by only one nucleotide (C vs. G) and reference Seq. Id. No. 16 **which has 100% sequence identity to the presently claimed Renilla GFP of Seq. Id. 2.** See e.g. Reference Seq. Id 15 and attached Result 4 DATABASE Alignment search; and Reference sequence Id. 16. . Bryan et al. teach the use of the bioluminescent green fluorescent proteins in cellular assays (e.g. live cells, including mammalian) and in high throughput screening systems (e.g. employing libraries) (e.g. see col. 2-3; 14). The Bryan reference further teaches the use of a "fusion partner" (e.g. a targetting agent) in its genetic fusion constructs. See e.g. col. 24. **Although teaching green fluorescent proteins from other sources e.g. *Aequorea victoria;*, the use of renilla green fluorescent proteins is "more ideal for use as an analytical tool" (e.g. see col. 4-5); see also patent claims directed to Renilla sequence Id 15 and 16.**

Thus, it would have been obvious to one of ordinary skill in the art at the time of applicant's invention to utilize the Bryan et al. polynucleotide Renilla green fluorescent protein (including seq. Id 15) in the Aran et al. genetic constructs for purposes of

performing screening assays (e.g. high throughput library screens) in order to obtain the benefits of the renilla protein in such assays as taught by the Bryan reference.

Discussion

Applicant's arguments directed to the above obviousness rejections over the Aran et al. and Bryan et al. references were considered but deemed nonpersuasive for the following reasons.

Applicant argues that "the Office has provided insufficient motivation ... to combine ... Bryan and Aran to provide a *Pitilosarcus* and *Renilla* GFP in a retroviral vector since the advantages described by the Aran reference address the advantages attributed to vectors containing *Aequoria* GFP and "[T]he applicants fail to see how this would motivate a skilled person to make a retroviral vector with a Renilla GFP since:

a. GFP's other than *Aequoria* GFP are not mentioned by Aran, and

b. at no point does Aran suggest other GFP's could be used in his vector.

These arguments were considered but deemed nonpersuasive for the following reasons.

Initially, it is noted that applicant's arguments regarding nonelected subject matter (e.g. Pitilosarcus) to the extent that they are not germaine to the above rejections, are not found persuasive. In this regard, Applicant's election without traverse of Group I (claims 1-9) and the species rGFP in Seq. Id. 1 in Paper No. 10 is again noted.

In response to applicant's argument that there is no suggestion to combine the references, the examiner recognizes that obviousness can only be established by

combining or modifying the teachings of the prior art to produce the claimed invention where there is some teaching, suggestion, or motivation to do so found either in the references themselves or in the knowledge generally available to one of ordinary skill in the art. See *In re Fine*, 837 F.2d 1071, 5 USPQ2d 1596 (Fed. Cir. 1988)and *In re Jones*, 958 F.2d 347, 21 USPQ2d 1941 (Fed. Cir. 1992).

Applicant's arguments that the Aran et al. Reference teaching is strictly limited to its example of vectors/cells comprising *Aequoria* GFP fails consider the Aran reference teaching as a whole which represents a generic teaching of the use of GFP's in general. For example, both the title and the abstract reference to GFP generically. E.g. "We have also incorporated the improved features of GFP as a reporter gene..." and the article nowhere limits its exemplified retoviral genetic construct, and the benefits thereof, as being specific only to *Aequoria* GFP . It is noted that the above rejections when referring to the Aran et al. teaching refer to *Aequoria* GFP as being exemplary of GFP's in general [" GFP gene (e.g. a red-shifted green fluorescent protein from *Aequorea victoria*) "] . Additionally, applicant has not provided any scientific rationale whatsoever as to why one of ordinary skill in the art would not have a reasonable expectation that the benefits of the exemplified retroviral *Aequoria* GFP construct is extrapolatable to other green fluorescent proteins, particularly *Renilla.*

Further, in response to applicant's arguments against the Aran reference individually, one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.*, 800 F.2d 1091, 231 USPQ

375 (Fed. Cir. 1986). In this regard, as pointed out in the above rejections, the Bryan reference teaches the interchangeability of the *Renilla* and *Aequoria* GFP's in vector constructs. Applicant is also directed to the above rejection citing "**Although teaching green fluorescent proteins from other sources e.g. *Aequorea victoria;*, the use of renilla green fluorescent proteins is "more ideal for use as an analytical tool" (e.g. see col. 4-5)"; and also patent claims directed to Renilla sequence Id 15 and 16.**

Accordingly, contrary to applicant's arguments, the above-cited references provide ample motivation for a skilled person to make a retroviral vector with a Renilla GFP

Accordingly, the above modified rejections are hereby maintained.

New Objection (s) and/or Rejection (s)

7. Claim 20 is rejected under 35 U.S.C. 103(a) as being unpatentable over the obviousness rejections using Aran et al. And Bryan et al. as applied to claims 1-3, 16 and 20 above, and, if necessary, further in view of Zolutukhin et al. US Pat. No. 5,874,304 (2/99: filed 1/96).

The above combined teaching of the Aran et al. and Bryan et al. References as described in the above obviousness rejections is hereby incorporated by reference in their entirety.

The reference differ from the presently claimed invention (e.g. claim 20) by failing to *explicitly* teach a human codon-optimized nucleic acid encoding a Renilla GFP (e.g. humanized GFP) in a retroviral vector.

However, Zolutukhin et al. teach that utilizing human codon-optimized nucleic acid GFP in nucleic acid constructs (including fusion proteins; e.g. col. 4 corresponding to present claim 2 "first gene" terminology) included in vectors (e.g. see col. 5, examples; particularly retroviral: see patent claims, especially claims 50 and 69) contained in cells (e.g. see patent claims 71-80) in which the constructs contain:

1. GFP (particularly Renilla: see col. 1 , last paragraph; col. 14 and Table 1; and especially col. 16, lines 3-15: "... spectrum of Renilla ... preferable to that of Aequorea);

2. IRES elements (e.g. see col. 13; particulary patent claims 50 and 62)

serves to overcome prior art obstacles and is advantageous (e.g. improved expression in mammalian and human cells) (e.g. see col. 1-2).

Accordingly, one of ordinary skill in the art at the time of applicant's invention would have been motivated to utilize "human codon-optimized nucleic acids expressing Renilla GFP in the genetic constructs (e.g. cells/vectors comprising renilla GFP/IRES elements) rendered obvious by the combined Aran et al. And Bryan et al. teaching in light of the advantages thereof imparted by such humanized sequences as taught by the Zolutukhin et al. reference.

Thus, it would have been prima facie obvious to one of ordinary skill at the time of applicant's invention to modify the cellular/vector genetic constructs taught by the Aran and Bryant reference to include human codon-optimized (e.g. humanized) nucleotides encoding renilla GFP in order to obtain the advantages thereof as taught by the Zolutukhin et al. reference.

8. Claims 1-3, 16 and 20 are rejected under 35 U.S.C. 103(a) as being unpatentable over Zolutukhin et al. US Pat. No. 5,874,304 (2/99: filed 1/96) and Bryan et al. US Pat. No. 6,232,107 (5/01: filed 10/98 or earlier)with attached Result 4 DATABASE Alignment search.

The Zolutukhin et al. reference teaches that utilizing human codon-optimized nucleic acid GFP in nucleic acid constructs (including fusion proteins; e.g. col. 4 corresponding to present claim 2 "first gene" terminology) included in vectors (e.g. see col. 5, examples; particularly retroviral: see patent claims, especially claims 50 and 69) contained in cells (e.g. see patent claims 71-80) in which the constructs contain:

1. GFP (particularly Renilla: see col. 1 , last paragraph; col. 14 and Table 1; and especially col. 16, lines 3-15: "... spectrum of Renilla ... preferable to that of Aequorea);

2. IRES elements (e.g. see col. 13; particulary patent claims 50 and 62)

servest to overcome prior art obstacles and is advantageous (e.g. improved expression in mammalian and human cells) (e.g. see col. 1-2).

Although the Zolutukhin et al. reference teaches nucleic acid which employ the preferential use of Renilla GFP the Zolutukhin reference differs from the presently claimed invention by failing to explicitly teach the use of a *Renilla* GFP gene sequence which encodes a GFP that is at least 90%, 95%, 100% identical to SEQ Id. 2.

Bryan et al. disclose and claim the use (e.g. diagnostics and "high throughput screening" e.g. libraries) of nucleic acid molecules encoding green fluorescent proteins (e.g. bioluminscent) from the genus Renilla, including reference Seq. ID No. 15 which is 98.4% (with best local similarity of 99.4%) homologous to elected seq. ID 1, differing by only one nucleotide (C vs. G) and reference Seq. Id. No. 16 **which has 100%**

sequence identity to the presently claimed Renilla GFP of Seq. Id. 2. See e.g. Reference Seq. Id 15 and attached Result 4 DATABASE Alignment search; and Reference sequence Id. 16. . Bryan et al. teach the use of the bioluminescent green fluorescent proteins in cellular assays (e.g. live cells, including mammalian) and in high throughput screening systems (e.g. employing libraries) (e.g. see col. 2-3; 14). The Bryan reference further teaches the use of a "fusion partner" (e.g. a targetting agent) in its genetic fusion constructs. See e.g. col. 24. **Although teaching green fluorescent proteins from other sources e.g. *Aequorea victoria;*, the use of renilla green fluorescent proteins is "more ideal for use as an analytical tool" (e.g. see col. 4-5); see also patent claims directed to Renilla sequence Id 15 and 16.**

Thus, it would have been obvious to one of ordinary skill in the art at the time of applicant's invention to utilize the Bryan et al. polynucleotide Renilla green fluorescent protein (including seq. Id 15) in the Zolutukhin reference. genetic constructs since:

a. Zolutukin teaches the preferential use of Renilla GFP thus motivating the selection of the functionally equivalent Bryan Renilla GFP obvious to one of ordinary skill in the art; and/or

b. one of ordinary skill in the art would have been motivated to select the Bryan reference Renilla sequences for r purposes of performing screening assays (e.g. high throughput library screens) in order to obtain the benefits of the renilla protein in such assays as taught by the Bryan reference.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Bennett Celsa whose telephone number is 703-305-7556. The examiner can normally be reached on 8-5.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Andrew Wang can be reached on 703-306-3217. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

Bennett Celsa
Primary Examiner
Art Unit 1639

BC